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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,058	05/08/2001	Kenneth C. Parker	SYP-172	2910

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EXAMINER
COOK, LISA V

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/851,058	Applicant(s) PARKER ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/11/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Please note that the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all correspondence regarding this application should be directed to Group Art Unit **1641**. All communications should be directed to **Lisa V. Cook**, whose telephone number is **(703) 305-0808**.

2. Claims 1-22 are pending and currently under consideration.

Sequence Compliance

3. Applicants response to the sequence non-compliance letter mailed 3/25/03 is acknowledged. The CRF has been entered.

Priority

4. No benefits of an earlier application are desired in the instant application.

Information Disclosure Statement

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PT0-1449 have cited the references they have not been considered.

6. The information disclosure statements filed in paper #4 on 8/8/01 has been considered as to the merits before first action.

Specification

7. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The instant abstract employs the term "said". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention..

A. In claims 1 and 13, the use of "substantially chemically identical" is vague and indefinite because it is not clear as to what the term "substantially" is intended to encompass. Are the two reagents chemically identical or not? Further it is not clear what if any difference between the two will be acceptable.

As recited the metes and bounds of the claim cannot be determined. The term is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Appropriate correction is required.

B. Claims 1 and 13 are vague and indefinite because the claims are drawn to a method reacting each protein sample with a different reagent of a reagent set. See claims 1 step (c) for example. This is ambiguous because it is not clear if the proteins are reacted with both reagents of the set of merely one. Please clarify.

C. Regarding claims 8 and 21, the phrase "including" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

D. Claims 8 and 21 are indefinite for being in improper Markush format. The Office recommends the use of the phrase "selected from the group consisting of...." with the use of the conjunction "and" rather than "or" in listing species. See MPEP 706.03(Y).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 1-3, 6-8, and 10-21 are rejected 35 U.S.C. 103(a) as being unpatentable over Aebersold et al. (WO 00/11208) in view of Sechi et al. (Analytical Chemistry, 1998, 70, 5150-5158).

Aebersold et al. teach methods of analyzing proteins or protein function in complex mixtures. The method utilizes a labeling compositions comprising the formula A-L-PRG. Wherein A represents an affinity label, PRG is a protein reactive group, and L is a linker group. This same formula is taught in the instant disclosure on page 8. The PRG selectively reacts with certain groups that are typically found in peptides (sulfhydryl, amino, carboxy, homoserine lactone groups). One or more affinity labeled reagents with different PRG groups is introduced into a mixture containing proteins. After protein A-L-PRG mixing the digestion is optional.

The PRG complex binds with the proteins of interest to produce a measurable tagged binding entity. This entity can subsequently be evaluated/analyzed via liquid chromatography/mass spectrometry (LC/MS). See abstract and page 8.

The method can be employed to screen and identify proteins, which are differential expressed in cells, tissue, or biological fluids. It is further possible to determine the absolute amount of the proteins utilizing known amounts of internal standards. See page 9 1st paragraph. The process is applicable in determining the state of protein modification, enzyme activity, and function. See pages 9-11.

Aebersold et al. differ from the instant invention in not specifically including a protein separation step involving gel electrophoresis in their method.

However, Sechi et al. disclose a method of combining gel electrophoresis (PAGE), mass spectrometric peptide mapping, and cysteine alkylation. Cysteine alkylation was used as a tool for the identification of cysteine-containing peptides. A 1:1 mixture of unlabeled acrylamide (non-deuterated peptide standard) and deuterium-labeled acrylamide (deuterated peptide standard), along with the proteins of interest were alkylated prior to electrophoresis separation. The peptide mixtures produced by trypsin digestion were analyzed by MADLI-TOF MS. The cysteine content information improved the protein identification process. See abstract and figure 3. Sechi et al. further disclose methods that would employ 1D Page and 2D Page protein separation. Page 5154 – 2nd column. The method allowed all proteins contained in the sample to be alkylated in a single step while all cysteines are homogenously alkylated with a single reagent prior to electrophoresis. Page 5154 1st column-last paragraph through 2nd column.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize electrophoresis separation along with deuterated/non-deuterated peptide standards and cysteine alkylation as taught by Sechi et al. to identify the protein and or protein fragments found in the method of Aebersold et al., because Sechi et al. taught that their method eliminated interference of advantageous acrylamide by modifying cysteine prior to electrophoresis (page 5154 1st column – 1st paragraph) and cysteine alkylation is required to ensure maximal coverage in MALDI-TOF MS peptide mapping of proteins isolated by PAGE (electrophoresis). The "information was readily obtained and used to improve the protein identification process". See abstract.

One of ordinary skill in the art would have been motivated to include protein separation via electrophoresis with cysteine alkylation in the mass spectrometry analysis procedure in order to acquire rapid and precise evaluation of proteins within a sample. See abstract.

II. Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aebersold et al. (WO 00/11208) in view of Sechi et al. (Analytical Chemistry, 1998, 70, 5150-5158) an in further view of Yates et al. (US Patent #5,538,897).

Please see Aebersold et al. (WO 00/11208) in view of Sechi et al. (Analytical Chemistry, 1998, 70, 5150-5158) as set forth above.

Aebersold et al. (WO 00/11208) in view of Sechi et al. (Analytical Chemistry, 1998, 70, 5150-5158) differ from the instant invention in not specifically teaching protein/peptide sequence via tandem mass spectrometry.

However, Yates et al. disclose a method of correlating a peptide fragment with amino acid sequences derived from a database. A peptide is analyzed by a tandem mass spectrometer to yield a peptide fragment mass spectrum (mass fingerprinting). A protein sequence database or a nucleotide sequence database is used to predict/identify the fragment. For each candidate sequence, a plurality (pool) of fragments of the sequences is identified and the masses-m/z ratios of the fragments are predicted and used to form a predicted mass spectrum. See abstract.

Aebersold et al. in view of Sechi et al. and Yates et al. are all analogous art because they are from the same field of endeavor, all three inventions teach methods involving protein fragment characterization and identification.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize tandem mass spectrometry database sequence comparison as taught by Yates et al. to identify the fragments found in the method of Aebersold et al. in view of Sechi et al. to evaluate a pool of modified protein sequences, because Yates et al. taught that the patented system for correlating fragment spectra with known sequences would avoid delay and/or subjectivity in hypothesizing or deducing candidate amino acid sequences from the fragment spectra. (Column 1 lines 44-62).

One having ordinary skill in the art would have been motivated to do this because in order to achieve maximal data processing/protein manipulation to determine the parameter of interest.

III. Claim 9 is rejected 35 U.S.C. 103(a) as being unpatentable over Aebersold et al. (WO 00/11208) in view of Sechi et al. (Analytical Chemistry, 1998, 70, 5150-5158) an in further of Bienvenut et al. (Analytical Chemistry, 1999, 71, 4800-4807).

Please see Aebersold et al. (WO 00/11208) in view of Sechi et al. (Analytical Chemistry, 1998, 70, 5150-5158) as set forth above.

Aebersold et al. (WO 00/11208) in view of Sechi et al. (Analytical Chemistry, 1998, 70, 5150-5158) differ from the instant invention in failing to teach transblotting and digestion combinations in protein identification.

Bienvenut et al. disclose methods of combining transblotting (OSDT) and in gel digestion of all proteins in parallel (PIGD) to increase the throughput of protein identification and characterization in proteome studies. Peptides liberated during transblotting of proteins through an immobilized trypsin membrane were trapped on a PVDF membrane and identified by mass spectrometry. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the OSDT/PIG combination procedure of Bienvenut et al. in the protein identification method of Aebersold et al. in view of Sechi et al., because Bienvenut et al. taught that the combination "led to greatly improved digestion of high molecular weight and basic proteins without loss of low molecular weight polypeptides. See abstract.

One of ordinary skill in the art would have been motivated to employ the combination procedure of Bienvenut et al. to take advantageous of an automated integrated system involving MALDI-TOF MS scanning, spectra treatment, protein identification, in order to generate a fully annotated 2-DE map. See page 4807.

IV. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Aebersold et al. (WO 00/11208) in view of Sechi et al. (Analytical Chemistry, 1998, 70, 5150-5158) an in further view of Clauser et al. (Proceedings of the National Academy of Sciences, USA, 1995, 92(11), 5072-6).

See Aebersold et al. (WO 00/11208) in view of Sechi et al. (Analytical Chemistry, 1998, 70, 5150-5158) as set forth above.

Aebersold et al. in view of Sechi et al. differ from the instant invention in not specifically teaching post-translational modification status of a protein/peptide by gel analysis.

However, Clauser et al. disclose a method involving mass spectrometry and two-dimensional polyacrylamide gel electrophoresis for the rapid identification and characterization of proteins. The method can detect and structurally characterize covalent modifications. The authors have characterized several post-translational modification and chemical modifications that may result from electrophoresis or subsequent sampling processing steps. The detection of these modifications is required in order to reliably and unambiguously establish the identify of each protein. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure post-translational protein modification as taught by Clauser et al. in the method of Aebersold et al. (WO 00/11208) in view of Sechi et al. (Analytical Chemistry, 1998, 70, 5150-5158) because Clauser et al. taught that the method allowed for the study cell-type dependent gene expression and large suites of cellular proteins with unprecedented speed and rigor. See abstract and page 5076.

10. For reasons aforementioned, no claims are allowed.

Remarks

11. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Gygi et al. (Nature Biotechnology, Vol.17, October 1999, pages 994-999) disclose a method of measuring individual proteins within complex mixtures. Specifically the method involves an ICAT (isotope-affinity tags) reagent DNA sequence.

B. Conrads et al. (Analytical Chemistry, 2000, 72, pages 3349-3354) disclose multiple analyses in a plurality of proteins mixtures employing mass spectrometry.

C. Yates et al. (US Patent # 6,017,693) disclose a method of correlating a peptide fragment mass spectrum with amino acid sequences derived from a database. Abstract.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
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7/24/03

LONG V. LE
SUPERVISORY PATENT EXAMINER
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07/25/03